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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,483	10/13/2000	Andreas Braun	24736-2033	7859

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BIOTECHNOLOGY LAW GROUP
c/o PORTFOLIO IP
P.O. BOX 52050
MINNEAPOLIS, MN 55402

EXAMINER	
CLOW, LORI A	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 07/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/687,483	BRAUN, ANDREAS	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,9-15,31-34,43,44,47-50,54 and 98-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,5,9-15,31-34,43,44,47-50,54 and 98-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/2/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED SUPPLEMENTAL ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicants' response, filed 2 March 2005, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 4, 5, 9-15, 31-34, 43, 44, 47-50, 54, and 98-128 are currently pending. Applicant is reminded that in future responses a listing of all claims, cancelled, pending, and new, must be present.

This action is supplemental to and replaces the non-final Office Action dated 4 April 2005.

Information Disclosure Statement

The Information Disclosure Statement filed 2 March 2005 has been considered. A signed copy of PTO Form 1449 is included with this Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4, 5, 9-15, 31, 43, 44, 47-50 and 109-128 are rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell et al. (WO 98/35609), further in view of Clausen et al. (Journal of Clinical Investigation (1996) Vol. 98, No. 5, pages 1195-1209).

Specifically, Campbell et al. teach a computer-based system for predicting the future health of an individual based upon acquiring and analyzing a number of biological and physiological biomarkers. The invention is directed toward providing a computer-based method and apparatus that provides an on-going system for assessing future health risks for a specific individual, and for monitoring the preventative measures taken so as to reduce the future health risks for that individual (page 6, lines 26-29).

In regard to claims 4, 43, 126, and 128 the system comprises a method of obtaining data from healthy members of the population. In particular, the term "specified biological condition" of the invention includes all ranges of health, from the most robustly healthy to the most severely diseased (page 22, lines 13-16). A plurality of biomarker values are obtained from each member of a larger test population (page 13, lines 3-4). The values are placed in a computer (see computer-system description on page 13) and the observations are associated with each member. These can be scalar or vector and imply an indexer (page 13, lines13-17). The database is stored on a computer-readable medium (page 13, lines 19-23; page 14, lines 3-4).

In regard to claims 5 and 44, the results are entered into the database and the samples can come from a variety of sources, such as saliva (body fluid), or toenails (biological sample), for example (page 16, lines 13-18).

In regard to claim 9, the database can comprise information on a variety of bio-markers, including nutritional and life-style bio-markers (page 16, lines 25-26). The total number of bio-

markers that may be used is unlimited in principal (page 19, lines 11-13). For example, if the biological condition is acquiring coronary heart disease within a specified time, serum cholesterol, glucose intolerance, systolic blood pressure, or cigarette smoking may be used as bio-markers (page 31, lines 23-28).

In regard to claims 10 and 47, the organisms of Campbell et al. are mammals (human patients; speaks of risks to persons, page 5).

In regard to claim 11, samples are collected from blood, blood fractions, cells, and organelles (see Table 1, beginning page 17).

In regard to claims 12-15 and 48-50, the data could be phenotypic data, physical data, or genotypic data (see page 9, biomarkers can be physiologic and biochemical).

In regard to claims 31, 109-125, 127, the database is contained in a computer system (page 13, lines 19-23).

Campbell et al. do not specifically teach only data from individuals that have not been pre-selected for any particular disease. However, Clausen et al. do teach that studying only healthy members of a population is beneficial. In particular, Clausen et al. studied the distribution of the insulin sensitivity index, the acute insulin response, and the glucose effect in young healthy Caucasians in effort to estimate the impact of anthropometric and environmental determinants on these variables (see abstract). It would have been prima facie obvious to one of ordinary skill in the art at the time of invention to have included only healthy individual data, as was acquired by Clausen et al., in the database of Campbell et al., as motivated by the statement that "it would be desirable if the onset of future health problems could be predicted for an individual with sufficient reliability far enough into the future so that the chances could be

increased for preventing future health problems for that individual rather that waiting for actual onset of a disease and then treating the symptoms (page 1, line 15-18; Campbell).

Claims 32-34, 98-100 and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0596205 A2 (Bullaughey et al.; Published 5 November 1994, PTO Form 1449, 20 February 2001, Reference BU), in view of Campbell et al. (WO 98/35609), in view of Clausen et al. (Journal of Clinical Investigation (1996) Vol. 98, No. 5, pages 1195-1209), in further view of US 5,498,545 (Vestal; published 12 March 1996; PTO Form 1449, 20 February 2001, Reference AI).

EP 0596205 A2 teaches an analytical system which is responsible for coordinating the operations of various hardware instruments in carrying out a bench method or bench sequence (see abstract). The bench hardware comprises a variety of instruments as well as a transport instrument.

In regard to claims 32, 33, 98-100 and 102 EP 0596205 A2 teaches a Bench Supervisor system such that a user can prepare a sample, and analyze the sample in the appropriate instrument. After the first method is complete, the system can pass the sample on to a next location for analysis (processing station equivalent). The next instrument, for example, could include a liquid chromatograph or a mass spectrometer chemstation (claim 33) (page 16, lines 1-16). The bench method assembles methods from the different instrument applications to process a sample from start to finish, in an uninterrupted process (page 16, lines 26-29). The bench system tracks the inputs and outputs from each instrument and passes the information along to the next instrument method (page 16, lines 26-28).

In regard to claim 34, EP 0596205 A2 does not specifically teach that the mass spectrometer chemstation includes analysis systems, however, it was well known to one of skill in the art at the time of the invention that a mass spectrometer system would include an analysis such that sample signals are analyzed and a quantitative result is obtained. This is evidenced by US 5,498,545 which teaches a system for analyzing multiple samples by mass spectrometry. The MALDI mass spectra system of the invention includes a step to convert time-of-flight spectrum into mass spectrum. Peaks are extracted and intensity of peaks analyzed. The computer interprets the results to yield, in this case, a sequence of bases in a DNA fragment (column 12, lines 47-58 and column 13, lines 7-11). It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to include such a system of MALDI spectrometry in the bench system of EP 0596205 A2, where the motivation is provided by US 5,498,545 to analyze multiple samples.

Claims 54 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0596205 A2 (Bullaughey et al.; Published 5 November 1994), in view of Campbell et al. (WO 98/35609), in further view of Clausen et al. (Journal of Clinical Investigation (1996) Vol. 98, No. 5, pages 1195-1209).

EP 0596205 A2 teaches a Bench Supervisor system such that a user can prepare a sample, and analyze the sample in the appropriate instrument. After the first method is complete, the system can pass the sample on to a next location for analysis (processing station equivalent). The next instrument, for example, could include a liquid chromatograph or a mass spectrometer chemstation (claim 33) (page 16, lines 1-16). The bench method assembles methods from the

different instrument applications to process a sample from start to finish, in an uninterrupted process (page 16, lines 26-29). The bench system tracks the inputs and outputs from each instrument and passes the information along to the next instrument method (page 16, lines 26-28).

While EP 0596205 A2 does not teach the database with healthy members, Campbell et al. do teach the database and Clausen et al. teach using healthy members, as recited above. EP 0596205 A2 provides the motivation to include the database of Campbell et al. (as recited above) in the analysis system by stating that the instruments include means for processing samples, transporting samples, and one or more resources to process the sample. The system may also advantageously include means for employing other programs to produce output data and a means for making decisions relative to the process sample, enabling the system to modify a method or re-direct a sample or change analysis of a function of an intermediate result (page 2, lines 50-55). It would therefore have been prima facie obvious to one of skill in the art at the time of the invention to include the database of Campbell and Clausen in the automated process system of EP 0596205 A2.

Claim 98 is rejected under 35 U.S.C. 103(a) as being unpatentable over Campbell et al. (WO 98/35609), in view of Clausen et al. (Journal of Clinical Investigation (1996) Vol. 98, No. 5, pages 1195-1209) in further view of US 5,498,545 (Vestal; published 12 March 1996).

As stated above Campbell et al. and Clausen et al. teach and make obvious a computer-based system for predicting the future health of an individual based upon acquiring and analyzing a number of biological and physiological biomarkers using data from healthy

individuals. The invention is directed toward providing a computer-based method and apparatus that provides an on-going system for assessing future health risks for a specific individual, and for monitoring the preventative measures taken so as to reduce the future health risks for that individual (page 6, lines 26-29).

Campbell et al. and Clausen et al. do not specifically teach that the bio-marker data come from a mass spectrometric analysis. However, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use mass spectrometer analysis of Vestal, who teaches a system for analyzing multiple samples by mass spectrometry (see abstract) on the samples included in the database of Campbell and Clausen. The motivation to do so is provided by Campbell et al. at page 20, line 20-23, which states that the use of biomarker data obtained from any source falls within the spirit and scope of the invention.

Claims 103-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0596205 A2 (Bullaughey et al.; Published 5 November 1994), in view of Campbell et al. (WO 98/35609), in view of Clausen et al. (Journal of Clinical Investigation (1996) Vol. 98, No. 5, pages 1195-1209), in view of US 5,498,545 (Vestal; published 12 March 1996) as applied to claims 100 and 102 above, in further view of US 6,602,662 B1 (Koster et al.; Published 5 August 2003; priority 18 March 1996; PTO 1449, 14 October 2003, Reference H).

EP 0596205 A2, Campbell, Clausen, and Vestal make obvious an analytical system which is responsible for coordinating the operations of various hardware instruments in carrying out a bench method or bench sequence wherein analysis systems comprise a mass spectrometer, as set forth above.

EP 0596206 A2, Campbell, Clausen, and Vestal do not specifically state that samples are analyzed by primer oligo base extension (PROBE), as required by claims 103-108. However, US 6,602,662 B1 does teach a mass-spectrometry based process for detecting nucleic acid molecules and sequences in the molecules which comprises hybridizing a nucleic acid molecule with a primer oligonucleotide that is complementary to a sequence that is adjacent to a region suspected of containing the target nucleotide; contacting the hybridized primer with dideoxynucleoside triphosphate and a polymerase to that it is extended onto the primer and; detecting the primer (see, for example, column 29; see claim 1). Column 13-14 further describes the methods whereby ligation and cleavage are used in nucleic acid detection. It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to use the PROBE method of Koster in mass spectrometry analysis in the system of EP 0596205 A2, Campbell, Clausen, and Vestal. The motivation being that the PROBE mass spectrometry method is particularly useful for diagnosing a predisposition to a disease or condition (column 3, lines 54-63) of Koster.

No claims are allowed.

Conclusion

Applicant's arguments with respect to the Campbell et al. reference are moot in view of the new grounds of rejection set forth above.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The

faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
6/22/05

June 20, 2005
Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow